Information Disclosure Statement

The Information Disclosure Statement is enclosed herewith.

Objections to the Specification

The specification was objected to for not containing a reference to the prior application as set forth in 37 CFR §1.62. Applicants have amended the specification to include a statement referring to the prior application as required by the Examiner. No new matter is added. Withdrawal of objection is respectfully requested.

The specification was objected to for not containing a Brief Description of the Drawings. Applicants have amended the specification to include a Brief Description of the Drawings. Support for the Brief Description of the Drawings can be found at page 50 (lines 16-20) [FIG. 1], page 50 (lines 21-24) [FIG. 2], page 52 (lines 2-4)[FIG. 3], pages 52 (lines 27-29) and 53 (lines 1, 3 and 4) [FIG. 4], page 53 (lines 1-4) [FIG. 5] and page 54 (lines 3-8) [FIG. 6] in the specification and inherently in the drawings. Thus, no new matter is added. Withdrawal of objection is respectfully requested.

Objections to the Drawings

The drawings are objected to by the Draftsperson under 37 CFR §1.84 and §1.152. Applicants respectfully disagree with the Draftsperson's objection and submit that Figures 1 and 2 are labeled correctly and in accordance with 37 CFR §1.84(h). Specifically, the Draftsperson stated that the current labels of Figures 1 and 2, ("FIG. 1" and "FIG. 2") should be labeled FIG. 1A-1I and FIG. 2A-2D, respectively. Applicants assert that nothing in 37 CFR §1.84(h) requires Applicants to label the figures in the manner suggested by the Examiner. Rather, 37 CFR §1.84(h)(2)(i) and (ii) simply requires that "[w]here views on two or more sheets form, in effect, a single complete view, the views on the sheets must be so arranged that the complete figure can be assembled without concealing any part of any of the view appearing on the various sheets" and that "[a] very long view may be divided into several parts placed one above the other on a single sheet...[so long as] the relationship between the different parts must be clear and unambiguous." Applicants submit that the current relationship is clear and unambiguous and contend that the current labels on Figures 1 and 2 comply with the relevant regulations.

Rejection under 35 U.S.C. §112(1)

Claims 29-35, 37, 39-42 stood rejected under 35 U.S.C. §112, first paragraph, for written description. Claims 29-35, 37, 39-42 have been cancelled and replaced with new Claims 69-91, thus obviating the rejection. Withdrawal of rejection is respectfully requested.

Rejection under 35 U.S.C. §112(2)

Claims 37, 42 and 57 stood rejected under 35 U.S.C. §112, second paragraph, for indefiniteness. Specifically, in rejecting Claim 37, the Examiner alleges that Applicant's use of the term "fusion protein" is vague as it is unclear as to the identity of the fusion partner of the fusion protein. Second, Claim 42 was rejected as indefinite because the Examiner alleged that it is unclear what Applicants meant by the phrase "suitable composition" and "suitable carrier." Third, in rejecting Claim 57 as indefinite, the Examiner alleges that the phrase "under conditions sufficient for the production of the encoded polypeptide" is indefinite. Claims 37, 42 and 57, along with rest of the pending claims, have been cancelled and replaced with new claims. Thus, the rejections have been obviated. However, because Applicants continue to employ the terms rejected on the basis of 35 U.S.C. §112, second paragraph in new claims, the Applicants will address the Examiner's rejection.

A. Claim 37

Claim 37 was rejected based on the Examiner's allegation that Claim 37 did not clearly point out the identity of the "fusion partner" of the claimed fusion protein. Claim 37 has been cancelled, but because Claim 79 also claims a fusion protein and is likely to face the same or a similar rejection in a later Office Action, Applicants will address the rejection. Applicants clearly identify potential a number of "fusion partners" in the specification. *See* specification p. 32, lines 19-29. According to the specification, adequate fusion partners include such proteins as lipoprotein D from *Haemophilus influenzae*, glutathione-S-transferase, and betagalactosidase but can be "any other relatively large co-protein which solubilizes the protein and facilitates production and purification" of the protein *See id.*

B. Claim 42

Claim 42 was rejected based on the Examiner's allegation that the phrases "suitable composition" and "suitable carrier" are unclear. Because, these two phrases are employed by Applicants in new claim 69, Applicants will address the rejection. Applicants submit that the

meaning of both phrases are clearly defined in the specification. Specifically, the phrases are clearly defined in the specification. Specifically, the phrases are defined in the specification's discussion surrounding the potential compositions and carriers that can be used in order to administer the polynucleotide into the subject in order to induce an immune response.

The specification clearly defines what is meant by a "suitable composition." Specifically, Applicants have described two such "suitable compositions." The first composition is a recombinant BASB024 polynucleotide that comprises DNA or RNA which encodes for or expresses an antigen of the BASB024 polynucleotide. *See* specification at 32, lines 8-17. The second such composition described consisted of a BASB024 polypeptide or fragment that is fused with a co-protein or chemical moiety which may or may not by itself produce antibodies but which is capable of stabilizing the first protein and, along with the fused protein, will have antigenic properties. *See* specification at 32, lines 19-23. Three co-proteins that can serve this purpose are mentioned in the specification; lipoprotein D from *Haemophilus influenzae*, Glutathione-S-transferase, and betagalactosidase. *See* specification at 32, lines 23-25.

In addition, the phrase "suitable carrier" is also clearly described in the specification. Specifically, Applicants have described two "suitable carriers." Because the preferred method of administration is through a subcutaneous, intramuscular, intravenous, or intradermal administration, a suitable carrier is an "aqueous or non-aqueous sterile injection solution[s] which may contain anti-oxidants, buffers, bacteristatic compounds and solutes which render the formulation isotonic with the bodily fluid...of the individual" and may also include a suspending agent. Applicants submit that one skilled in the art, when viewed in context with and with guidance from the specification, would not find either the phrase "suitable composition" or "suitable carrier" unclear or ambiguous.

C. Claim 57

Claim 57 was rejected because, according to the Examiner, it contained an unclear phrase. Because the phrase "under conditions sufficient for the production of the encoded polypeptide" is employed by Applicants in new claim 73, Applicants will address the rejection. The meaning of this phrase would be clear to one in the art, particularly in light of the description of the conditions outlined in the specification. Specifically, such "conditions sufficient for the production of the encoded polypeptide" were described as:

> [A vector comprising the polynucleotide of SEQ. ID NO:2 was then] introduced into the E. coli strain Novablue (DE3), in which, the gene for the T7 polymerase is placed under the control of the isoprpyl-beta D thiogalactoside (IPTG)-regulatable lac promoter...[and] grown at 37° C under agitation until the optical density at 600nm (OD600) reached 0.6. At that time-point, IPTG was added at a final concentration of 1mM and the culture was grown for 4 additional hours.

See specification, page 51, Example 2. These conditions are what the present invention claims as "conditions sufficient for the production of the encoded polypeptide. Applicants submit that this phrase is clear to one skilled in the art.

Rejection under 35 U.S.C. §102(b)

Claim 29-32, 37, 39-4, and 57 were rejected under 35 U.S.C. §102(b) as being anticipated by two different references. Applicants respectfully disagree and request that the Examiner withdraw the rejection.

A. Claims 29, 37, 39, 40 and 41 Anticipated by Legrain et al.

Claims 29, 37, 39, 40 and 41, stood rejected under 35 U.S.C. §102(b) as being anticipated by Legrain et al.[2] based on the Examiner's allegation that the claims were "drawn to an immunogenic fragment of amino acid that matches an aligned contiguous segment of SEQ. ID NO:4 with no more than five single amino acid substitutions." Claims 29, 37, 39, 40, and 41 have been cancelled. Further, the Examiner's rejection is not applicable to the new claims 61-91. Withdrawal of rejection is respectfully requested.

B. Claim 57 Anticipated by Legrain et al.

Claim 57 has also been rejected as being anticipated by Legrain et al.[3] Claim 57 has been cancelled. Withdrawal of rejection is respectfully requested.

C. Claims 29-32, 37, 39 and 40-41 Anticipated by Bash et al.

Claim 29-32, 37, 39 and 40-41 stood rejected as being anticipated by Bash et al.[4] The Examiner based his rejection on allegations that:

> Bash et al. teach immunogenic fragements of polypeptides isolated from outer membrane proptein of *Neisseria Meningitidis*. Bash et al. teach antigenic

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[2] *See* 130 GENE 73-80 (1993)

[3] *See id.*

[4] *See* Bash et al., 63 INFECTION AND IMMUNITY 4:1484-90 (1995)

> epitopes isolated from 14 different serotypes and strains of Neisseria meningitidis. The prior art teaches the claimed invention...[as] [f]ragments comprising 15 or 20 amino acid[s] matching an aligned contiguous segment of SEQ ID NO:4 would be inherent in the outer membrane proteins taught by the prior art.

The Examiner's conclusion that an aligned contiguous segment of SEQ ID NO:4 would be inherent in the outer membrane proteins taught by the prior art is faulty. An Examiner must provide rationale or evidence tending to show inherency. *See* MPEP 2112. "Inherency...may not be established by probabilities or possibilities [and] [t]he mere fact that a certain thing may result from a given set of circumstances is not sufficient." *See id.*; *see also In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). Rather, the Examiner's analysis "must provide a basis in fact and/or technical reasoning to reasonably support" his conclusions. *See id.* In this case, the Examiner provides no reasonable support - the Office Action merely states that Bash et al. teaches antigenic epitopes isolated from 14 different serotypes of *Neisseria Meningitidis*, the same genus and species as Applicants are using. Instead, the Examiner's analysis is based purely on speculation. Basing a rejection on claims 29-32, 37, 39 and 40-41, as well as new claims 69-91, on such speculation is clearly improper. Thus, Applicants respectfully request the withdrawal of rejection.

CLOSING REMARKS

Allowance of the pending claims is respectfully requested.

FEE DEFICIENCY

☒ If an extension of time is deemed required for consideration of this paper, please consider this paper to comprise a petition for such an extension of time. The Commissioner is hereby authorized to charge the fee for any such extension to Deposit Account No. 50-0258.

and/or

☒ If any additional fee is required for consideration of this paper, please charge Account No. 50-0258.

Respectfully submitted,

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Appendix A - Pending Claims

69. An isolated polypeptide comprising a member selected from the group consisting of

(a) an amino acid sequence matching SEQ ID NO:4 and

(b) an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids that matches an identically aligned contiguous segment of SEQ ID NO:4,

wherein the isolated polypeptide, when administered to a subject in a suitable composition which can include an adjuvant, or a suitable carrier coupled to the polypeptide, induces an antibody or T-cell immune response to a polypeptide having the sequence of SEQ ID NO:4.

70. An isolated polynucleotide encoding a polypeptide of Claim 69 or the full complement to the isolated polynucleotide.

71. The isolated polypeptide of claim 69, wherein the polypeptide is according to (a).

72. An isolated polynucleotide encoding a polypeptide of Claim 71 or the full complement to the isolated polynucleotide.

73. A process for expressing the polynucleotide of Claim 72 comprising transforming a host cell with an expression vector comprising the polynucleotide and culturing the host cell under conditions sufficient for expression of the polynucleotide.

74. The isolated polypeptide of claim 69, wherein the polypeptide is according to (b).

75. An isolated polynucleotide encoding a polypeptide of Claim 74 or the full complement to the isolated polynucleotide.

76. The isolated polypeptide of claim 69, wherein the immunogenic fragment of (b) comprises at least 20 amino acids.

77. The isolated polypeptide of claim 69, wherein the isolated polypeptide consists of SEQ ID NO:4.

78. An isolated polynucleotide encoding the polypeptide of Claim 77 or the full complement to the isolated polynucleotide.

79. A process for expressing the polynucleotide of Claim 78 comprising transforming a host cell with an expression vector comprising the polynucleotide and culturing the host cell under conditions sufficient for expression of the polynucleotide.

80. A fusion protein comprising the isolated polypeptide of Claim 69.

81. An isolated polynucleotide comprising the polynucleotide of SEQ ID NO:3.

82. An isolated polynucleotide segment comprising a polynucleotide sequence or the full complement of the entire length of the polynucleotide sequence, wherein the polynucleotide sequence hybridizes to the full complement of SEQ ID NO:3 minus the complement of any stop codon, wherein the hybridization conditions include incubation at 42°C in a solution comprising: 50% formamide, 5x SSC (150mM NaCl, 15mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 micrograms/ml denatured, sheared salmon sperm DNA, followed by washing in 0.1x SSC at 65°C; and, wherein the polynucleotide sequence is identical to SEQ ID NO:3 minus any terminal stop codon, except that, over the entire length corresponding to SEQ ID NO:3 minus any terminal stop codon, $\mathbf{n_n}$ nucleotides are substituted, inserted or deleted, wherein $\mathbf{n_n}$ satisfies the following expression

$$\mathbf{n_n \leq x_n - (x_n \bullet y)}$$

wherein $\mathbf{x_n}$ is the total number of nucleotides in SEQ ID NO:3 minus any terminal stop codon, **y** is at least 0.95, and wherein any non-integer product of $\mathbf{x_n}$ and **y** is rounded down to the nearest integer before subtracting the product from $\mathbf{x_n}$; and wherein the polynucleotide sequence detects *Moraxella catarrhalis*.

83. An expression vector comprising the isolated polynucleotide of Claim 70.

84. A host cell transformed with the expression vector of Claim 83.

85. A vaccine comprising the polypeptide of Claim 69 and a pharmaceutically acceptable carrier.

86. The vaccine of Claim 85, wherein the vaccine comprises at least one other *Moraxella catarrhalis* antigen.

87. An antibody immunospecific for the polypeptide or immunogenic fragment of Claim 69.

88. A method for inducing an immune response in a mammal comprising administration of the polypeptide of Claim 69.

89. A method of diagnosing a *Moraxella catarrhalis* infection, comprising identifying a polypeptide of Claim 69, or an antibody that is immunospecific for the polypeptide, present within a biological sample from an animal suspected of having such an infection.

90. A method for inducing an immune response in a mammal comprising administration of the isolated polynucleotide of Claim 70.

91. A therapeutic composition useful in treating humans with *Moraxella catarrhalis* comprising at least one antibody directed against the polypeptide of claim 69 and a suitable pharmaceutical carrier.

Appendix B: Brief Description of the Drawings

FIG. 1 represents the alignment of the BASB024 polynucleotide sequence.

FIG. 2 represents the alignment of the BASB024 polypeptide sequence.

FIG. 3 represents a coomassie staining and Anti-His Immuno-staining of the expression and purification of recombinant BASB024 in *E. coli.*

FIG. 4 represents a coomassie stained SDS-PAGE of the purification fractions of BASB024.

FIG. 5 represents a western blot of purified recombinant BASB024 protein probed with anti-His antibody.

FIG. 6 represents a western blot showing anti-BASB024 antibodies in human convalescent sera using native BASB024 into the gel.

Appendix C: Abstract to the Disclosure

The invention provides BASB024 polypeptides and polynucleotides encoding BASB024 polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are diagnostic, prophylactic and therapeutic uses.